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Visual Impairment and Blindness Avoided with Ranibizumab in Hispanic and Non-Hispanic Whites with Diabetic Macular Edema in the United States

Rohit Varma, MD, MPH,[1] *Neil M. Bressler, MD,*[2] *Quan V. Doan, PharmD,*[3] *Mark Danese, PhD,*[3] *Chantal M. Dolan, PhD,*[4] *Abraham Lee, BA,*[3] *Adam Turpcu, PhD*[4]

Objective: To estimate visual impairment (VI) and blindness avoided with intravitreal ranibizumab 0.3 mg treatment for central-involved diabetic macular edema (DME) among Hispanic and non-Hispanic white individuals in the United States.

Design: Population-based model simulating visual acuity (VA) outcomes over 2 years after diagnosis and treatment of DME.

Participants: Visual acuity changes with and without ranibizumab were based on data from the RISE, RIDE, and DRCR Network trials.

Methods: For the better-seeing eye, VA outcomes included VI, defined as worse than 20/40 in the better-seeing eye, and blindness, defined as VA of 20/200 or worse in the better-seeing eye. Incidence of 1 or both eyes with central-involved DME in 2010 were estimated based on the 2010 United States population, prevalence of diabetes mellitus, and 1-year central-involved DME incidence rate. Sixty-one percent of incident individuals had bilateral DME and 39% had unilateral DME, but DME could develop in the fellow eye.

Main Outcomes Measures: Cases of VI and blindness avoided with ranibizumab treatment.

Results: Among approximately 102 million Hispanic and non-Hispanic white individuals in the United States 45 years of age and older in 2010, an estimated 37 274 had central-involved DME and VI eligible for ranibizumab treatment. Compared with no ranibizumab treatment, the model predicted that ranibizumab 0.3 mg every 4 weeks would reduce the number of individuals with VI from 11 438 (95% simulation interval [SI], 7249–16 077) to 6304 (95% SI, 3921–8981), a 45% (95% SI, 36%–53%) reduction at 2 years. Ranibizumab would reduce the number of incident eyes with VA worse than 20/40 from 16 910 (95% SI, 10 729–23 577) to 9361 (95% SI, 5839–13 245), a 45% (95% SI, 38%–51%) reduction. Ranibizumab was estimated to reduce the number of individuals with legal blindness by 75% (95% SI, 58%–88%) and the number of incident eyes with VA of 20/200 or worse by 76% (95% SI, 63%–87%).

Conclusions: This model suggests that ranibizumab 0.3 mg every 4 weeks substantially reduces prevalence of VI and legal blindness 2 years after initiating treatment among Hispanic and non-Hispanic white individuals in the United States with central-involved DME that has caused vision loss. *Ophthalmology 2015;122:982-989 © 2015 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

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Diabetic retinopathy and diabetic macular edema (DME) are the leading causes of vision loss in working-age adults in the United States.[1] In persons with diabetes mellitus, severe vision loss usually is associated with proliferative diabetic retinopathy, whereas the leading cause of moderate vision loss, a loss of 15 letters or more (doubling of the visual angle), is macular edema.[2] Macular edema is characterized by swelling of the macula, the central part of the retina that mediates high-resolution vision.[3] In the Early Treatment Diabetic Retinopathy Study, the risk of moderate vision loss from clinically significant macular edema assigned to no treatment unless and until high-risk proliferative diabetic retinopathy developed was 33% after 3 years of follow-up.[2] Until recently, laser photocoagulation, as applied in the Early Treatment Diabetic Retinopathy Study, was the standard of care for treatment of clinically significant macular edema because it reduced the risk of 15-letter or more loss (approximately 3 lines or more of visual acuity [VA] on an Early Treatment Diabetic Retinopathy Study chart) by 50%.[2] However, 15% of treated patients were estimated to lose vision,[2] and in recent trials evaluating focal/grid laser treatment among patients with some vision

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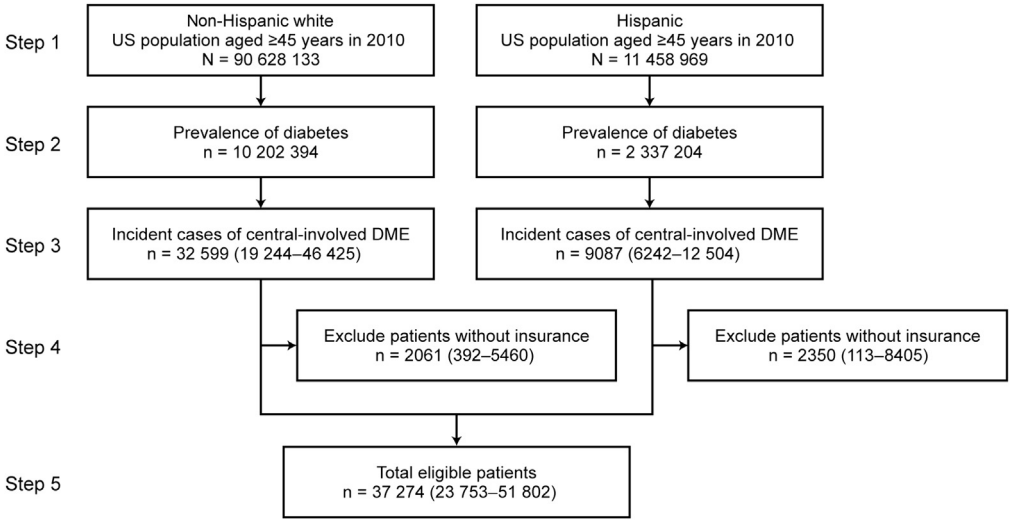

Figure 1. Flowchart showing the estimated total number of persons 45 years of age and older with central-involved diabetic macular edema (DME) causing vision of 20/32 or worse approximate Snellen equivalent who would be considered for ranibizumab treatment in the United States in 2010.

loss associated with DME, vision improvement was estimated to occur in only approximately 30% of patients.[4] More recent study results show that intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents have been shown to have a greater chance of avoiding vision loss and improving vision.[4–6]

Given the impact of ranibizumab (Lucentis; Genentech, Inc., South San Francisco, CA) on VA in patients with DME, we undertook this study to estimate the number of non-Hispanic white and Hispanic persons with DME in the United States who may be able to avoid vision loss and blindness with the use of ranibizumab treatment.

Methods

A population-based effectiveness model was developed to simulate changes in VA with versus without treatment with ranibizumab 0.3 mg administered every 4 weeks in patients with central-involved DME and VA of 20/32 or worse approximate Snellen equivalent (defined as best-corrected VA [BCVA] letter score of ≤78). Eyes with central-involved DME but with vision better than 20/32 approximate Snellen equivalent were assumed not to be candidates for ranibizumab treatment at this time. Specifications for model parameters are listed in Table 1.

Estimate of Patients with Central-Involved Diabetic Macular Edema for Whom Ranibizumab Treatment Would Be Considered

The steps carried out to estimate the total number of patients with central-involved DME in the United States for whom ranibizumab treatment would be considered at this time are summarized in Figure 1. First, only non-Hispanic white and Hispanic individuals were considered in the model because the incidence of DME was available for these groups, but not for other racial or ethnic groups. Using data from the 2010 United States Census Bureau, individuals 45 years of age and older were stratified into 10-year age groups.[7] In step 2, the prevalence of self-reported diabetes was obtained from National Health and Nutrition Examination Survey 2005 through 2008 data.[8] Next (step 3), the 1-year incidence of central-involved DME for non-Hispanic white individuals was derived from the Wisconsin Epidemiologic Study of Diabetic Retinopathy,[9] and that for Hispanics was derived from the Los Angeles Latino Eye Study (LALES).[10] Cases of DME that did not involve the center of the macula or VA better than 20/32 approximate Snellen equivalent in the incident eye were excluded. The proportion of incident eyes with central-involved DME that had VA 20/32 or worse approximate Snellen equivalent (BCVA letter score ≤78) was estimated using data from LALES. Because we did not have access to the Wisconsin Epidemiologic Study of Diabetic Retinopathy data, the same proportion of incident eyes with central-involved DME with VA 20/32 or worse approximate Snellen equivalent from LALES was applied for non-Hispanic white individuals. Next (step 4), individuals without health insurance were excluded by assuming that they were unlikely to have access to ranibizumab. The percentage of the uninsured United States population by age and race or ethnic groups was derived from a population survey conducted by the United States Census Bureau in 2010.[11] Finally (step 5), the total number of persons eligible for treatment was derived by summing across all age and race or ethnic groups. This final number then was used to simulate treatment with and without ranibizumab 0.3 mg. These methods were repeated for treatment with ranibizumab 0.5 every 4 weeks.

Estimated Rates of Visual Impairment and Blindness

The 2-year rates of visual impairment (VI) and blindness for both the better-seeing eye and the incident eye were estimated using a person-level simulation. Visual impairment was defined as BCVA letter score of 68 or fewer in the better-seeing eye, that is, an approximate Snellen equivalent worse than 20/40.[12] Legal blindness was defined as a BCVA letter score of 38 or fewer in the better-seeing eye, that is, an approximate Snellen equivalent 20/200 or worse.[12]

The model was conducted as a 2-dimensional Monte Carlo simulation to account for various sources of patient-level variability and parameter uncertainty using TreeAge Pro 2009 software (TreeAge Software, Inc., Williamstown, MA). To achieve stable rates, 300 averages of 280 simulated patients (based on the sample size of relevant patients in A Study of Ranibizumab Injection in Subjects with Clinically Significant Macular Edema